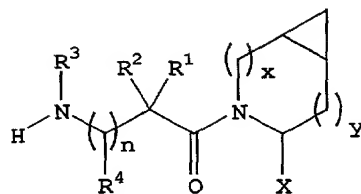


What is Claimed is:

1. A compound having the structure



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herein x is 0 or 1 and y is 0 or 1, provided that

x = 1 when y = 0 and

x = 0 when y = 1; and wherein

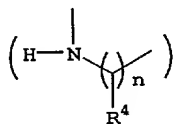
n is 0 or 1;

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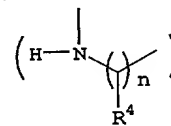
X is H or CN;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are the same or different and are independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, hydroxytricycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl; all optionally substituted through available carbon atoms with 1, 2, 3, 4 or 5 groups selected from hydrogen, halo, alkyl, polyhaloalkyl, alkoxy, haloalkoxy, polyhaloalkoxy, alkoxy carbonyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, polycycloalkyl, heteroarylamino, arylamino, cycloheteroalkyl, cycloheteroalkylalkyl, hydroxy, hydroxyalkyl, nitro, cyano, amino, substituted amino, alkylamino, dialkylamino, thiol, alkylthio, alkylcarbonyl, acyl, alkoxy carbonyl, aminocarbonyl, alkynylaminocarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, alkylsulfonylamino, alkylaminocarbonylamino, alkoxy carbonylamino, alkylsulfonyl, aminosulfinyl, aminosulfonyl, alkylsulfinyl, sulfonamido or sulfonyl;

- and  $R^1$  and  $R^3$  may optionally be taken together to form  $-(CR^5R^6)_m-$  where  $m$  is 2 to 6, and  $R^5$  and  $R^6$  are the same or different and are independently selected from hydroxy, alkoxy, H, alkyl, alkenyl, alkynyl, cycloalkyl, halo, amino, substituted amino, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxy carbonylamino, aryloxy carbonylamino, alkoxy carbonyl, aryloxy carbonyl, or alkylaminocarbonylamino, or  $R^1$  and  $R^4$  may optionally be taken together to form  $-(CR^7R^8)_p-$  wherein  $p$  is 2 to 6, and  $R^7$  and  $R^8$  are the same or different and are independently selected from hydroxy, alkoxy, cyano, H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, halo, amino, substituted amino, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl, cycloheteroalkylalkyl, alkylcarbonylamino, arylcarbonylamino, alkoxy carbonylamino, aryloxy carbonylamino, alkoxy carbonyl, aryloxy carbonyl, or alkylaminocarbonylamino, or optionally  $R^1$  and  $R^3$  together with

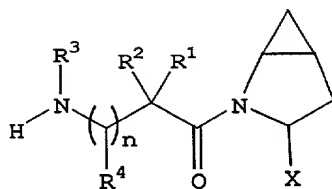


from a 5 to 7 membered ring containing a total of 2 to 4 heteroatoms selected from N, O, S, SO, or SO<sub>2</sub>;

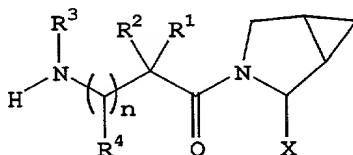


- or optionally  $R^1$  and  $R^3$  together with form a 4 to 8 membered cycloheteroalkyl ring wherein the cycloheteroalkyl ring has an optional aryl ring fused thereto or an optional 3 to 7 membered cycloalkyl ring fused thereto;
- including all stereoisomers thereof;
- and a pharmaceutically acceptable salt thereof, or a prodrug ester thereof, and all stereoisomers thereof.

2. The compound as defined in Claim 1 having the structure:

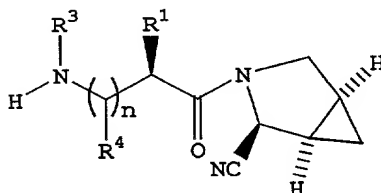


5 3. The compound as defined in Claim 1 having the structure:



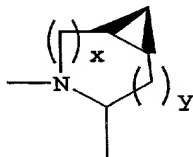
10 4. The compound as defined in Claim 1 having the structure:

15 5. The compound as defined in Claim 1 having the structure:



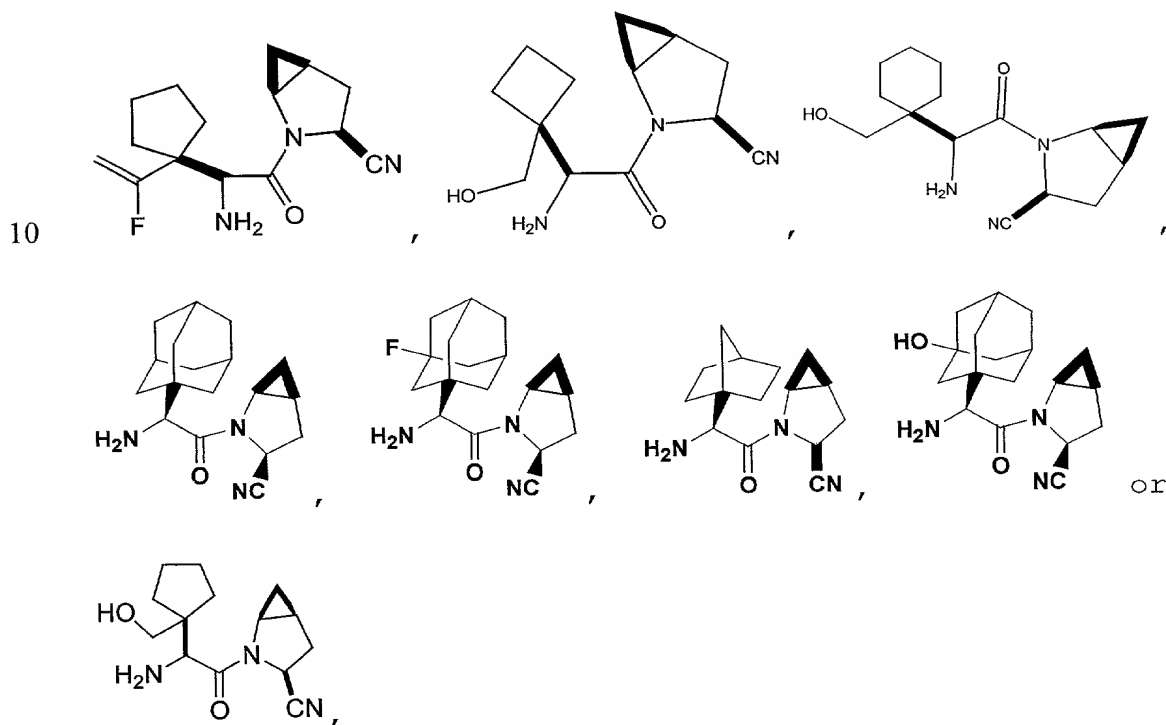
20 6. The compound as defined in Claim 1 wherein:  
 $R^3$  is H,  $R^1$  is H, alkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, alkylcycloalkyl, hydroxyalkyl, hydroxyalkylcycloalkyl, hydroxycycloalkyl, hydroxybicycloalkyl, or hydroxytricycloalkyl,  
 $R^2$  is H or alkyl, n is 0,  
 25 X is CN.

7. The compound as defined in Claim 1 wherein the cyclopropyl fused to the pyrrolidine has the configuration:



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8. The compound as defined in Claim 1 having the structure:



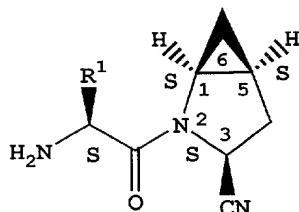
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or a pharmaceutically acceptable salt thereof.

9. The compound as defined in Claim 8 wherein the pharmaceutically acceptable salt is the hydrochloride salt or the trifluoroacetic acid salt.

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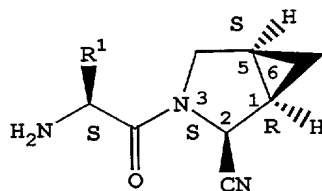
10. The compound as defined in Claim 1 which is



A

(1S, 2(2S), 3S, 5S)

wherein R<sup>1</sup> is alkyl, cycloalkyl, bicycloalkyl,  
 5 tricycloalkyl, alkylcycloalkyl, hydroxyalkyl,  
 hydroxycycloalkyl, hydroxyalkylcycloalkyl,  
 hydroxybicycloalkyl, or hydroxytricycloalkyl,  
 or



B

(1R, 2S, 3(2S), 5S)

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wherein R<sup>1</sup> is alkyl, cycloalkyl, bicycloalkyl,  
 tricycloalkyl, alkylcycloalkyl, hydroxyalkyl,  
 hydroxycycloalkyl, hydroxyalkylcycloalkyl,  
 hydroxybicycloalkyl, or hydroxytricycloalkyl.

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11. A pharmaceutical composition comprising a  
 compound as defined in Claim 1 and a pharmaceutically  
 acceptable carrier therefor.

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12. A pharmaceutical combination comprising a DP4  
 inhibitor compound as defined in Claim 1 and an  
 antidiabetic agent other than a DP4 inhibitor for  
 treating diabetes and related diseases, an anti-obesity  
 agent and/or a lipid-modulating agent.

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13. The pharmaceutical combination as defined in  
 Claim 12 comprising said DP4 inhibitor compound and an  
 antidiabetic agent.

14. The combination as defined in Claim 13 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR  $\gamma$  agonist, a PPAR  $\alpha/\gamma$  dual agonist, an SGLT2 inhibitor, an aP2 inhibitor, a glycogen phosphorylase inhibitor, an AGE inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1) or mimetic thereof, insulin and/or a meglitinide.

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15. The combination as defined in Claim 14 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, Exendin-4, LY307161, NN2211, and/or LY315902.

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16. The combination as defined in Claim 13 wherein the compound is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 100:1.

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17. The combination as defined in Claim 12 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta compound, an anorectic agent, and/or a fatty acid oxidation upregulator.

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18. The combination as defined in Claim 17 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, famoxin, and/or mazindol.

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19. The combination as defined in Claim 12 wherein the lipid modulating agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, an ACAT inhibitor, a cholesteryl ester transfer protein inhibitor, or an ATP citrate lyase inhibitor.

20. The combination as defined in Claim 19 wherein the lipid modulating agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, implitapide, CP-529,414, avasimibe, TS-962, MD-700, and/or LY295427.

21. The combination as defined in Claim 19 wherein the DP4 inhibitor is present in a weight ratio to the lipid-modulating agent within the range from about 0.01 to about 100:1.

22. A pharmaceutical combination comprising a DP4 inhibitor compound as defined in Claim 1 and an agent for treating infertility, an agent for treating polycystic ovary syndrome, an agent for treating a growth disorder and/or frailty, an anti-arthritis agent, an agent for preventing inhibiting allograft rejection in transplantation, an agent for treating autoimmune disease, an anti-AIDS agent, an agent for treating inflammatory bowel disease/syndrome, an agent for treating anorexia nervosa, an anti-osteoporosis agent and/or an anti-obesity agent.

23. A method for treating diabetes, insulin resistance, hyperglycemia, hyperisulinemia, or elevated blood levels of free fatty acids or glycerol, obesity, Syndrome X, dysmetabolic syndrome, diabetic complications, hypertriglyceridemia,

hyperinsulinemia, atherosclerosis, impaired glucose homeostasis, impaired glucose tolerance, infertility, polycystic ovary syndrome, growth disorders, frailty, arthritis, allograft rejection in transplantation,

5 autoimmune diseases, AIDS, intestinal diseases, inflammatory bowel syndrome, nervosa, osteoporosis, or an immunomodulatory disease or a chronic inflammatory bowel disease, which comprises administering to a mammalian species in need of treatment a therapeutically effective

10 amount of a compound as defined in Claim 1.

24. The method as defined in Claim 23 for treating type II diabetes and/or obesity.

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